#### REMARKS

Upon entry of the above amendment, claims 1-12, 14 and 16-17 will be pending in the captioned application. The claims have been amended to incorporate the hydrates, solvates, salts, hydrates of the salts and solvates of the salts of the compounds of formula 1. Specific basis for this amendment can be found at page 5, lines 8-11.

The amendments to the claims do not introduce new matter within the meaning of 35 U.S.C. §132. Accordingly, the Examiner is respectfully requested to enter the above amendment before examination. If the Examiner has any questions regarding this submission, she is invited to telephone the undersigned attorney.

Respectfully submitted, NATH & ASSOCIATES PLLC

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Date: February 3, 2005

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# DT05 Rec'd PCT/PT0 0 3 FEB 2005.

## Appendix A

## Claim Amendments

1. (Currently amended) Compounds A compound of formula 1,

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in which

R1 and R2 represent independently from one another hydrogen or 1-4C-alkyl, or R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur sulfur atom,

R9 is  $-(CH_2)_m-S(O)_2-R10$ ,  $-(CH_2)_n-C(O)-R11$  or  $-(CH_2)_p-Z-(CH_2)_q-R14$ ,

R10 is -N(R12)R13,

R11 is -N(R12)R13,

- R12 and R13 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, or R12 and R13 together, and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring,
- Z represents a bond, -O-, -C(O)-, -C(O)-N(H)-, -N(H)-C(O)- or  $-S(O)_2-$ ,
- R14 is hydrogen, hydroxyl, 1-4C-alkoxy, hydroxy-2-4C-alkoxy, 1-4C-alkoxy-1-4C-alkoxy, 1-4C-alkoxycarbonyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl, 1-4C-alkylcarbonyl or 1-4C-alkylcarbonylamino,
- m is an integer from 1 to 4,
- n is an integer from 1 to 4,
- p is an integer from 1 to 4,
- q is an integer from 1 to 4,

and the salts of these compounds or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

2. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 represent independently from one another hydrogen or 1-4C-alkyl, or R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a spiro-linked

cyclopentane, cyclohexane, tetrahydrofurane or tetrahydropyran ring,

R9 is  $-(CH_2)_m-S(O)_2-R10$ ,  $-(CH_2)_n-C(O)-R11$  or  $-(CH_2)_p-Z-(CH_2)_q-R14$ ,

R10 is -N(R12)R13,

R11 is -N(R12)R13,

R12 and R13 are independent from each other hydrogen or 1-4C-alkyl, or R12 and R13 together, and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring,

Z represents a bond, -0- or  $-S(0)_2-$ ,

R14 is hydrogen, 1-4C-alkoxy, 1-4C-alkoxy-1-4C-alkoxy, 1-4C-alkoxycarbonyl, aminocarbonyl, mono- or di-1-4C-alkylaminocarbonyl or 1-4C-alkylcarbonylamino,

n is 1 or 2,

m is 1 or 2,

p is 1, 2 or 3,

q is 1 or 2,

3. (Currently amended) Compounds  $\underline{A}$  compound of formula 1 according to claim 1, in which

either

R1 is hydrogen and

R2 is hydrogen,

or

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy,

R7 is methyl and

R8 is hydrogen,

R9 is  $-(CH_2)_m-S(O)_2-R10$ ,  $-(CH_2)_n-C(O)-R11$  or  $-(CH_2)_p-Z-(CH_2)_q-R14$ ,

R10 is -N(R12)R13,

R11 is -N(R12)R13,

R12 and R13 are independent from each other hydrogen or 1-4C-alkyl, or R12 and R13 together, and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring,

Z represents -0- or - $S(0)_2$ -,

R14 is hydrogen, 1-4C-alkoxy or 1-4C-alkoxy-1-4C-alkoxy,

n is 1 or 2,

m is 1 or 2,

p is 1, 2 or 3,

q is 1 or 2,

and the salts of these compounds or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

4. (Currently amended) Compounds  $\underline{A}$  compound of formula 1 according to claim 1, in which

either

R1 is hydrogen and

R2 is hydrogen,

or

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formula (a)

wherein

R4 is methoxy,

R5 is methoxy,

R9 is dimethylaminocarbonylmethyl, aminocarbonylmethyl, piperidin-1-ylcarbonylmethyl or morpholino-4-ylcarbonylmethyl,

5. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formula (a)

wherein

R4 is methoxy,

R5 is methoxy,

R9 is aminocarbonylmethyl or isopropylaminocarbonylmethyl, and the salts of these compounds or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

6. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur sulfur atom,

R9 is  $-(CH_2)_n-C(O)-R11$ ,

R11 is -N(R12)R13,

R12 and R13 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, or R12 and R13 together, and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring,

n is an integer from 1 to 4,

7. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formulae (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a spiro-linked cyclopentane, cyclohexane, tetrahydrofurane or tetrahydropyran ring,

R9 is  $-(CH_2)_n-C(O)-R11$ ,

R11 is -N(R12)R13,

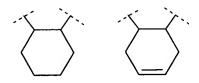
R12 and R13 are independent from each other hydrogen or 1-4C-alkyl, or R12 and R13 together, and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring,

n is 1 or 2,

and the salts of these compounds or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

8. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from



R3 represents a phenyl derivative of formula (a)

wherein

R4 is 1-4C-alkoxy,

R5 is 1-4C-alkoxy,

R9 is  $-(CH_2)_n-C(O)-R11$ ,

R11 is -N(R12)R13,

R12 is hydrogen and

R13 is hydrogen or 1-4C-alkyl,

n is 1 or 2,

and the salts of these compounds or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

9. (Currently amended) Compounds A compound of formula 1 according to claim 1, in which

R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

R3 represents a phenyl derivative of formula (a)

wherein

R4 is methoxy,

R5 is methoxy,

R9 is  $-(CH_2)_n-C(O)-R11$ ,

R11 is -N(R12)R13,

R12 is hydrogen and

R13 is hydrogen or isopropyl,

m is 1,

10. (Currently amended) Compounds A compound of formula 1 according to claim 1 one of the claims 1 to 9 in which R1 and R2 together, and with inclusion of the two carbon atoms[[,]] to which they are bonded, form a group selected from

and in which the hydrogen atoms in the positions 4a and 8a are cis-configurated, or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

- 11. (Currently amended) Compounds A compound of formula 1 according to claim 10 in which the absolute configuration (according to the rules of Cahn, Ingold and Prelog) is S in the position 4a and R in the position 8a, or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.
- 12. (Currently amended) Compounds A compound of formula 1 according to one of the claims 1 to 4 and 6 to 7 claim 1, in which R3 represents a phenyl derivative of formula (a),

or a hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

### 13. (Canceled)

14. (Currently amended) Pharmaceutical compositions containing A pharmaceutical composition comprising one or more compounds of formula 1 according to claim 1, or a pharmaceutically acceptable hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof, together with the usual a pharmaceutical auxiliaries and/or carrier materials auxiliary and/or excipient.

#### 15. (Canceled)

16. (Currently amended) A method for treating an illness treatable by the administration of a PDE4 inhibitor in a patient comprising administering to said patient in need thereof a therapeutically effective amount of a compound of formula 1 as claimed in claim 1, or a pharmaceutically acceptable hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

17. (Currently amended) A method for treating <u>an</u> airway disorders disorder in a patient comprising administering to said patient <u>in need thereof</u> a therapeutically effective amount of a compound of formula 1 as claimed in claim 1, or a pharmaceutically acceptable hydrate, solvate, salt, hydrate of a salt or solvate of a salt thereof.

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# Appendix B

## Abstract of the Disclosure

The compounds of a certain formula (1),

$$\begin{array}{c|c}
 & O^{-} \\
 & N^{+} \\
 & R9
\end{array}$$

$$\begin{array}{c|c}
 & R9
\end{array}$$

$$\begin{array}{c|c}
 & R9
\end{array}$$

$$\begin{array}{c|c}
 & R3
\end{array}$$

$$\begin{array}{c|c}
 & R1
\end{array}$$

$$\begin{array}{c|c}
 & R1
\end{array}$$

in which the given substituents have the meanings as given in the description, are novel effective PDE4 inhibitors.